

In the Claims:

Please amend the claims as follows:

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1. **(Currently Amended)** A vector system for selectively packaging a replication defective adenovirus nucleic acid sequence in an adenovirus capsid based on adenovirus serotype, the vector system comprising:

- (a) a first adenovirus nucleic acid sequence comprising:
- (i) 5' and 3' adenovirus inverted terminal repeats (ITRs);
  - (ii) a first adenovirus serotype-specific cis-acting packaging sequence; and
  - (iii) a heterologous nucleic acid operably linked to a transcriptional control sequence;

(b) a second adenovirus nucleic acid sequence comprising:

- (i) 5' and 3' adenovirus ITRs;
- (ii) a second adenovirus serotype-specific cis-acting packaging sequence,

wherein the second adenovirus nucleic acid fails to encode a 52/55 kDa trans-acting protein specific for the second cis-acting packing sequence; and

(c) an adenovirus 52/55 kDa trans-acting protein that supports packaging of the first adenovirus nucleic acid sequence and fails to support packaging of the second adenovirus nucleic acid sequence,

wherein the replication defective adenovirus comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof.

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2. **(Previously Amended)** The vector system of claim 1, wherein the adenovirus capsid, packaging and 52/55 kDa protein encoding sequences are human adenovirus sequences.

3. **(Previously Amended)** The vector system of claim 1, wherein the first and second adenovirus serotype-specific cis-acting packaging sequences are selected from the group consisting of adenovirus type 2 (Ad2), adenovirus type 5 (Ad5), adenovirus type 7 (Ad7), adenovirus type 12 (Ad12), adenovirus type 17 (Ad17), and adenovirus type 40 (Ad40) packaging sequences.

4. (Previously Amended) The vector system of claim 3, wherein the first adenovirus serotype-specific cis-acting packaging sequence is from adenovirus type 5 and the second adenovirus serotype-specific cis-acting packaging sequence is from adenovirus type 7.
5. (Previously Amended) The vector system of claim 3, wherein the first adenovirus serotype-specific cis-acting packaging sequence is from adenovirus type 7 and the second adenovirus serotype-specific cis-acting packaging sequence is from adenovirus type 5.
6. (Previously Amended) The vector system of claim 1, wherein the first adenovirus nucleic acid sequence fails to produce a complete adenovirus capsid.
7. (Previously Amended) The vector system of claim 6, wherein the first adenovirus sequence is encapsidated in a capsid comprising at least one polypeptide encoded by the second adenovirus sequence.
8. (Previously Amended) The vector system of claim 6, wherein the first adenovirus sequence is packaged in a capsid encoded by the second adenovirus sequence.
9. (Previously Amended) The vector system of claim 42, wherein the replication defective adenovirus comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene or combination thereof.
10. (Original) The vector system of claim 1, wherein the failure to produce a functional 52/55 kDa trans-acting protein is due to a mutation in the sequence encoding the protein.
11. (Original) The vector system of claim 10, wherein the mutation is a missense mutation, a point mutation, a frameshift mutation or a deletion mutation.
12. ~~(Canceled)~~

D<sup>2</sup> 13. **(Currently Amended)** The vector system of claim 1, wherein the adenovirus 52/55 kDa trans-acting protein that supports packaging of the [helper-dependent] first adenovirus nucleic acid sequence is encoded by a nucleic acid sequence functionally-associated with the genome of an adenovirus replication competent host cell.

14. (Original) The vector system of claim 13, wherein adenovirus replication competent host cell is a 293 cell line.

15-16. ~~(Canceled)~~

17. **(Currently Amended)** A vector system for selectively packaging a replication defective adenovirus nucleic acid sequence in an adenovirus capsid based on adenovirus serotype, the vector system comprising:

- D<sup>3</sup>
- (a) a first adenovirus nucleic acid sequence comprising:
    - (i) 5' and 3' adenovirus ITRs;
    - (ii) a first adenovirus serotype-specific cis-acting packaging sequence; and
    - (iii) a heterologous nucleic acid operably linked to a transcriptional control sequence;
  - (b) a second adenovirus nucleic acid sequence comprising:
    - (i) 5' and 3' adenovirus ITRs;
    - (ii) a second adenovirus serotype-specific cis-acting packaging sequence; and
    - (iii) a nucleic acid sequence encoding an adenovirus 52/55 kDa trans-acting protein

that supports packaging of the first adenovirus nucleic acid sequence and fails to support packaging of the second adenovirus nucleic acid sequence,

wherein the replication defective adenovirus comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof.

18. (Previously Amended) A vector system for selectively packaging a replication defective adenovirus nucleic acid sequence in an adenovirus capsid based on adenovirus serotype, the vector system comprising:

- (a) a first adenovirus nucleic acid sequence comprising:
    - (i) 5' and 3' adenovirus ITRs;
    - (ii) a first adenovirus serotype-specific cis-acting packaging sequence; and
    - (iii) a heterologous nucleic acid operably linked to a transcriptional control sequence;
  - b) a second adenovirus nucleic acid sequence comprising:
    - (i) 5' and 3' adenovirus ITRs;
    - (ii) a second adenovirus serotype-specific cis-acting packaging sequence,wherein the second adenovirus nucleic acid fails to encode a 52/55 kDa protein specific for the second cis-acting packing sequence; and
  - (c) a cell comprising a nucleic acid sequence encoding adenovirus serotype 52/55 kDa trans-acting protein specific for the first cis-acting packing sequence,  
wherein the replication defective adenovirus comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof.
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19. (Currently Amended) A vector system for selectively packaging a replication defective adenovirus nucleic acid sequence in an adenovirus capsid based on adenovirus serotype, the vector system comprising:

- D<sup>af</sup>
- (a) a first adenovirus nucleic acid sequence comprising:
    - (i) 5' and 3' adenovirus ITRs;
    - (ii) a first adenovirus serotype-specific cis-acting packaging sequence; and
    - (iii) a heterologous nucleic acid operably linked to a transcriptional control sequence;
  - (b) a second adenovirus nucleic acid sequence comprising:
    - (i) 5' and 3' adenovirus ITRs;
    - (ii) a second adenovirus serotype-specific cis-acting packaging sequence,wherein the [helper] first adenovirus nucleic acid fails to encode a polypeptide having the activity of the [helper] first adenovirus serotype 52/55 kDa trans-acting protein; and

(c) an expression cassette comprising a nucleic acid sequence encoding adenovirus serotype 52/55 kDa trans-acting protein specific for a first adenovirus serotype-specific cis-acting packaging sequence,

wherein the replication defective adenovirus comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof.

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20. (Previously Amended) A vector comprising a replication defective adenovirus sequence comprising:

- (a) a first adenovirus serotype-specific cis-acting packaging sequence; and
- (b) a nucleic acid sequence encoding a functional second adenovirus serotype-specific 52/55 kDa protein, wherein said protein is not specific for the first adenovirus serotype-specific cis-acting packaging sequence,

wherein the replication defective adenovirus sequence comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof.

21. (Original) The vector of claim 20, further comprising at least one adenoviral nucleic acid sequence needed to produce an adenoviral capsid.

22. (Original) The vector of claim 21, further comprising sufficient adenoviral nucleic acid sequence to produce a complete adenoviral capsid when the vector is expressed in an adenovirus replication-competent host cell.

23. (Previously Amended) The vector of claim 20, wherein the first adenovirus serotype-specific cis-acting packaging sequence and second adenovirus serotype-specific a nucleic acid sequence are selected from the group consisting of adenovirus type 2 (Ad2), adenovirus type 5 (Ad5), adenovirus type 7 (Ad7), adenovirus type 12 (Ad12), adenovirus type 17 (Ad17), and adenovirus type 40 (Ad40).

24. (Previously Amended) The vector of claim 23, wherein the first adenovirus serotype sequence is adenovirus type 5 and the second adenovirus serotype sequence is adenovirus type 7.

25. (Previously Amended) The vector of claim 23, wherein the first adenovirus serotype sequence is adenovirus type 7 and the second adenovirus serotype sequence is adenovirus type 5.

26. (Previously Amended) A transformed or isolated infected cell comprising the vector system of claim 1, claim 17, claim 18, claim 19 or the vector of claim 20.

D<sup>5</sup>  
27. (**Currently Amended**) A kit useful for making adenovirus encapsidated replication defective nucleic acid sequences, the kit comprising [carrier means being compartmentalized to receive in close confinement therein] one or more containers comprising a vector system of claim 1, claim 17, claim 18 or claim 19.

28-30. (Canceled)

31. (**Currently Amended**) A method of producing a replication defective encapsidated adenovirus vector, comprising the following steps:

(a) transforming or infecting into adenovirus replication competent host cells

(i) a first adenovirus nucleic acid sequence comprising:

5' and 3' adenovirus inverted terminal repeats (ITRs);

a first adenovirus serotype-specific cis-acting packaging sequence; and

a heterologous gene operably linked to a transcriptional control sequence;

(ii) a second adenovirus nucleic acid sequence comprising:

5' and 3' adenovirus ITRs;

a second adenovirus serotype-specific cis-acting packaging sequence,

wherein the second adenovirus nucleic acid fails to encode a 52/55 kDa protein specific for the second adenovirus serotype-specific cis-acting packaging sequence; and

(iii) a nucleic acid sequence encoding an adenovirus 52/55 kDa protein specific for a first adenovirus serotype-specific cis-acting packaging sequence; and

(b) culturing the cells under conditions where the first replication defective adenovirus sequence is encapsidated to produce a replication defective adenovirus vector,

wherein the replication defective adenovirus comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof.

32. **(Currently Amended)** A method of producing a replication defective encapsidated adenovirus vector, comprising the following steps:

(a) transforming or infecting into an adenovirus replication competent host cell a first and second adenovirus replication defective sequences, wherein the cell comprises a nucleic acid sequence encoding an adenovirus 52/55 kDa trans-acting protein that supports packaging of a first adenovirus nucleic acid sequence and fails to support packaging of a second adenovirus nucleic acid sequence, and wherein

(i) the first adenovirus nucleic acid sequence comprises:

5' and 3' adenovirus inverted terminal repeats (ITRs);  
a first adenovirus serotype-specific cis-acting packaging sequence; and  
a heterologous gene operably linked to a transcriptional control sequence;

(ii) the second adenovirus nucleic acid sequence comprises:

5' and 3' adenovirus ITRs;  
a second adenovirus serotype-specific cis-acting packaging sequence,  
wherein the second adenovirus nucleic acid fails to encode a 52/55 kDa trans-

acting protein specific for the second adenovirus serotype-specific cis-acting packaging sequence; and

(b) culturing the cells under conditions where the first replication defective adenovirus sequence is encapsidated to produce a replication defective adenovirus vector,

wherein the replication defective adenovirus comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof.

33. **(Currently Amended)** A method of producing a replication defective encapsidated adenovirus vector, comprising the following steps:

(a) transforming or infecting a first and second adenovirus replication defective sequences into an adenovirus replication competent host cell, wherein

(i) the first adenovirus nucleic acid sequence comprises:

5' and 3' adenovirus inverted terminal repeats (ITRs);

a first adenovirus serotype-specific cis-acting packaging sequence;

a heterologous gene operably linked to a transcriptional control sequence; and

a nucleic acid sequence encoding an adenovirus 52/55 kDa protein specific for the

first adenovirus serotype-specific cis-acting packaging sequence; and

(ii) the second adenovirus nucleic acid sequence comprises:

5' and 3' adenovirus ITRs;

a second adenovirus serotype-specific cis-acting packaging sequence,

wherein the second adenovirus nucleic acid fails to encode a 52/55 kDa trans-acting protein specific for the second adenovirus serotype-specific cis-acting packaging sequence; and

(b) culturing the cells under conditions where the first replication defective adenovirus sequence is encapsidated to produce a replication defective adenovirus vector,

wherein the replication defective adenovirus comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof.

34. **(Previously Amended)** The method of claim 31, 32, or 33 wherein the second adenovirus sequence further comprises an adenoviral nucleic acid sequence encoding a complete adenoviral viral capsid.

35. **(Previously Amended)** A vector for selectively packaging replication defective nucleic acid sequences in adenovirus capsids, the vector comprising:

(a) a replication defective adenovirus sequence comprising an adenovirus serotype 7 (Ad7) cis-acting packaging sequence;



- (b) a nucleic acid sequence encoding an adenovirus serotype 5 (Ad5) 52/55 kDa protein; and
- (c) an adenoviral nucleic acid sequence that encodes a viral capsid and fails to encode or produce an adenovirus 7 serotype 52/55 kDa trans-acting protein.

✓  
36-39. (Canceled)

40. **(Currently Amended)** A packaging cell line for selectively packaging a replication defective adenovirus nucleic acid sequence in an adenovirus capsid, the cell line comprising:

- (a) a first adenovirus nucleic acid sequence comprising:
  - (i) 5' and 3' adenovirus inverted terminal repeats (ITRs);
  - (ii) a first adenovirus serotype-specific cis-acting packaging sequence; and
  - (iii) a heterologous nucleic acid operably linked to a transcriptional control sequence;
- (b) a second adenovirus nucleic acid sequence comprising:
  - (i) 5' and 3' adenovirus ITRs;
  - (ii) a second adenovirus serotype-specific cis-acting packaging sequence,wherein the second adenovirus nucleic acid fails to encode a 52/55 kDa trans-acting protein specific for the second adenovirus serotype-specific cis-acting packaging sequence; and
- (c) an adenovirus 52/55 kDa trans-acting protein specific for the first adenovirus serotype-specific cis-acting packaging sequence,

wherein the replication defective adenovirus comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof.

41. **(Currently Amended)** A packaging cell line for selectively packaging a replication defective adenovirus nucleic acid sequence in an adenovirus capsid, the cell line comprising:

- (a) a nucleic acid sequence encoding an adenovirus serotype-specific 52/55 kDa trans-acting protein;
- (b) a first adenovirus nucleic acid sequence comprising:
  - (i) 5' and 3' adenovirus inverted terminal repeats (ITRs);

- (ii) a first adenovirus serotype-specific cis-acting packaging sequence; and
- (iii) a heterologous nucleic acid operably linked to a transcriptional control sequence;
- (c) a second adenovirus nucleic acid sequence comprising:
  - (i) 5' and 3' adenovirus ITRs;
  - (ii) a second adenovirus serotype-specific cis-acting packaging sequence that fails to support the activity of the adenovirus serotype-specific 52/55 kDa trans-acting protein, wherein the replication defective adenovirus comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof.

42. **(Currently Amended)** A vector system for selectively packaging a replication defective nucleic acid sequence in an adenovirus capsid, the vector system comprising:

- D<sup>7</sup>
- (a) a first adenovirus nucleic acid sequence comprising:
    - (i) 5' and 3' viral inverted terminal repeats (ITRs);
    - (ii) a first adenovirus serotype-specific cis-acting packaging sequence; and
    - (iii) a heterologous nucleic acid operably linked to a transcriptional control sequence, wherein the first adenovirus nucleic acid fails to produce a 52/55 kDa trans-acting protein specific for the first adenovirus serotype-specific cis-acting packaging sequence;
  - (b) a second adenovirus nucleic acid sequence comprising:
    - (i) 5' and 3' virus ITRs;
    - (ii) a second adenovirus serotype-specific cis-acting packaging sequence, wherein the second adenovirus nucleic acid fails to produce a 52/55 kDa trans-acting protein specific for the second adenovirus serotype-specific cis-acting packaging sequence; and
  - (c) a nucleic acid encoding an adenovirus serotype-specific 52/55 kDa trans-acting protein that supports packaging of the first adenovirus serotype-specific cis-acting packaging sequence and fails to support packaging of the second adenovirus serotype-specific cis-acting packaging sequence.
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